

An HPC-Based Approach to Study Living System Computational Model Parameter Dependency

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Abstract. High performance computing (HPC) allows one to run in parallel large amount of independent numerical experiments for computationally intensive simulations of a complex system. Results of such experiments can be used to derive dependencies between functional characteristics of simulated system and parameters of the computational model. In this paper, we implemented this HPC approach with using a computational model of the electrical activity in the left ventricle of human heart. To illustrate possibilities of the approach, we analyzed dependencies of electrophysiological characteristics of the left ventricle on the parameters of its geometry. Particularly, we identified a dependence of the dynamics of activated myocardium part during excitation on the model parameters of the myocardial fiber orientation in the ventricular wall.

Keywords: high performance computing · parallel computing · heart simulation

1 Introduction

Modern progress in systems biology and high performance computing (HPC) have made it possible to perform computer simulations of the physiological functions of complex living systems. Such simulation can be utilized to derive the dependencies between hidden, unobservable in clinical data parameters and functional characteristics of the systems. These dependencies can be used for solving the inverse problem and make the clinical diagnostics better.

However, deriving such dependencies for computational models of complex living system is complicated process because simulation requires long time and contemporary models have large number of parameters that influence functional characteristics. To solve this problem, we developed an HPC-based approach to study the parameter dependency of living system models.

According to suggested approach, large amount of independent numerical experiments for computationally intensive simulations are executed on HPC cluster

in parallel. The simulation results are used to derive dependencies between functional characteristics of simulated system and parameters of the computational model.

The approach could be used even for the simulation software that is not support parallel computing, because large amount of independent simulation tasks with different parameter values are executed on the HPC cluster.

To illustrate possibilities of the approach, we analyzed dependencies of electrophysiological characteristics of the left ventricle (LV) of human heart on the parameters of its geometry.

2 An HPC-based Approach to Study Computational Model Parameter Dependency

Our approach is based on the execution of large amount of independent simulation tasks on computational cluster (each task with different parameter values) and statistical analysis of simulation results. We assume that simulation software for the investigated computational model is already exists. In addition, we assume that simulation takes a few hours or days. Hence, the parallel computing support for one simulation task is not necessary.

The approach consists of the following steps:

1. Choosing a set of model parameters that we plan to change and determining the functional characteristics that are dependent on those parameters.
2. Determining the domain of parameters values, which will be used during the experiments, and preparing the input data for the simulation software.
3. Performing simulation on the HPC cluster. Large amount of independent computational tasks using existing simulation software with different parameter values are executed in parallel (embarrassing parallelism).
4. Performing statistical analysis of experiment results. The results are represented in the form $y^j = f(x_1^j, x_2^j, \dots, x_N^j)$, where f is the dependency between parameters and functional characteristic. To determine the form and coefficients of the dependencies we use the regression analysis method.

This research approach gives us some advantages in comparison with qualitative descriptions of experiments. First, the obtained result is a function. A type of this function presents a hypothesis regarding the process behavior, and its coefficients can be used for distinguishing criterion that separate normal and pathological cases. In addition, through the principal component analysis, we can find physiological parameters the mostly affecting on processes. Second, the approach provides the possibility to restore hidden parameters of the physiological system from clinical data.

3 Implementation

To be able to use the suggested approach, we implemented the software system that executes tasks on the computational cluster, collects the results, and

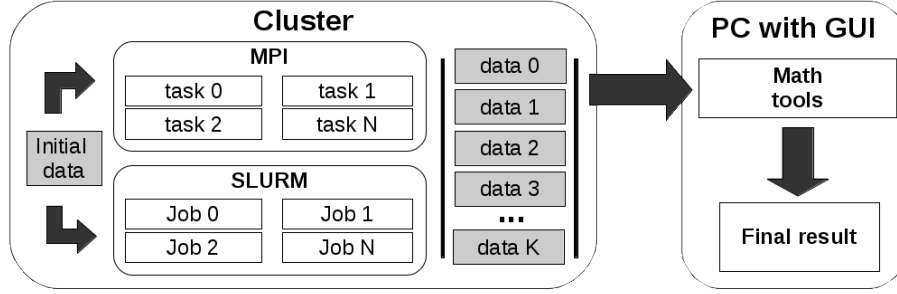


Fig. 1: Architecture of system with *MPI* or *SLURM*

provides tools for statistical analysis and visualization. The architecture of the system is shown in Fig. 1.

Two types of parallel execution of the simulation tasks on the cluster are implemented: based on *MPI* and *SLURM* resource manager tools.

The *MPI* implementation is based on the master-slave concept with load balancing over task queue. This implementation shows itself to be well, but when applying in more complicated experiments, cause several problem. When some combination of parameters leads to insoluble problem formulations the simulation software quits unexpectedly. This, in turn, can lead to an unexpected end of all *MPI* tasks. We do not describe this complex experiment in the paper.

The *SLURM* implementation is the most convenient, as an error in one task has no effect on other tasks. Furthermore, the *SLURM*'s task distribution is more flexible in comparison with the *MPI* implementation.

For reduction of the output data, the simulation software must be compiled as a library and wrapped in Python with module *ctypes*. Result arrays are saved in a hard drive in compressed binary file through standard numpy command `savez_compressed`. The wrapper structure is shown in Fig. 2.

After this, a data is moved into the machine with GUI and is processed by modules *numpy* and *scipy*.

This approach allows us to divide numerical experiments and results processing, for maximal flexibility of our research.

4 Computational Experiments

In order to illustrate the possibilities of our approach, we analyzed dependences of electrophysiological characteristics of the LV on the parameters of its geometry. Particularly, we identified a dependence of the dynamics of activated myocardium part during excitation on the model parameters of the myocardial fiber orientation in the ventricular wall.

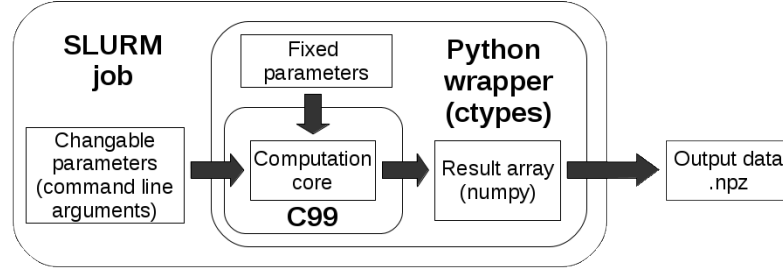


Fig. 2: SLURM and Python wrapper above C (C99) code.

4.1 LV Models

The research is based on the continuum description of the LV tissue. The simulation includes an anatomical model for description of the shape and the fiber direction, and an electrophysiological models for description of the excitation properties of the LV tissue. The Euler method is used for calculation.

Anatomical model: We used a simplified anatomical model, which was developed in our group earlier [3]. The anatomical shape parameters are fixed: LV height $Z_b = 60$ mm, wall thickness on apex $h = 8$ mm, radius from the axis to epicardium on base $R_b = 33$ mm, wall thickness on base $L_b = 12$ mm, and curvature $\varepsilon = 0.85$. Only parameters γ_0, γ_1 are changed. This parameters influence on fiber direction in the LV. In addition, the anatomical model provide a method for generate a structured grid. This grid is used for calculate electrophysiological differential equation by Euler's method.

Electrophysiological model: We use the Aliev-Panfilov [1] model for simulation of the electrophysiological activity of the heart myocardium at the cellular level. The model equations are represented as follows:

$$\begin{aligned} \dot{u} &= -ku(u - a)(u - 1) - uv + \nabla \cdot (D\nabla u) \\ \dot{v} &= \eta(u)(8u - v) \end{aligned}$$

where $\eta(u) = 0.1$ if $u > a$ and $\eta(u) = 1$ if $u \leq 1$; $k = 8$, $a = 0.03$. For introducing the material anisotropy, we used a symmetrical diffusion tensor: $D_{11} = 12$, $D_{22} = 1.33$, $D_{12} = D_{21} = 0.0$. Thus, the excitation wave propagation speed along the fibers is 3 times faster than across them.

Initial activation The model does not account the conduction system of the heart. We used the initial activation on endocardium apex applying the model coordinates: $\psi \geq 0.7 \cdot \frac{\pi}{2}, \gamma \geq 0.6$. This solution is based on the previous work [4].

In our experiments, we used an existing implementation of these models [6] in C language with OpenMP support.

4.2 Experiment Protocol

During the experiment, we measured a part of the excited myocardium of the LV depending on the time for every model. For every point of the electrical mesh, we calculated the corresponding myocardium volume and the arrival time of the excitation wave. The part of the excited myocardium $V_{\text{act}}(t)$ is a percent of the activated LV before the instant t . The choice of this parameter is connected with the fact that the transmural angle of fibers has influence on this parameter. In practice, it can be calculated through the activation of the ventricle's map during the physiological experiment or clinical electrophysiological study of the heart. Moreover, $V_{\text{act}}(t)$ may be interpreted as the index of myocardium activation coherence.

We selected parameters γ_0 and γ_1 for changing in the series of numerical experiment. These parameters determine the fiber direction in the LV. Parameters of influence on the ventricle's shape stayed fixed.

For calculation of $V_{\text{act}}(t)$, the time interval of the wave spread $[0, T_{\text{max}}]$ is divided into 10,000 parts. For every sub-interval $[t_k, t_k + 1)$, we calculated the activated volume as sum of activated point volumes. The activated myocardium volume at the instant t is calculated as the sum of volumes in groups $t_1, \dots, t_k + 1$, if $t \in [t_k, t_k + 1]$. Thus, the arrival time of waves into activated points group is equal to average arrival time of wave in these points. So, we get two sequences of data 10,000 elements in each. X_{time} is an average time of point groups' activation. Y_{vol} is the volume of activated myocardium in time moment X_{time} .

4.3 Results

After computation of the X_{time} and Y_{vol} sequences, we use the ordinary least squares (OLS) method. The Levenberg–Marquardt algorithm was used for finding the minimum of the OLS discrete functional. We tried to use polynomials, logarithmic, sedate, and exponential regression for function approximation. Finally, we have selected the 4-th degree polynomial (1). The value p_0 is fixed on first activated points group's level: in this case it matches the initial activation. The results of approximation are shown in Fig. 3.

$$V_{\text{act}}(t) = p_4 t^4 + p_3 t^3 + p_2 t^2 + p_1 t^1 + p_0 \quad (1)$$

For coefficients p_0, p_1, p_2, p_3 , we searched dependence on the initial changeable parameters γ_0 and γ_1 . By analogy with previous variants, we use the least square method and the Levenberg – Marquardt algorithm.

$$p_i = B_3^i \gamma_1 \gamma_0 + B_2^i \gamma_1 + B_1^i \gamma_0 + B_0^i \quad (2)$$

Approximation by the polynomial (2) is the most simple and accurate. Results are shown on Fig.(4). The final formulas are represented below in the Results section.

We insert coefficients of equation (2) into (3) to get the final equation (3), that describes the activated myocardium volume dependence. This equation is based on 55 experiments, and has the following form:

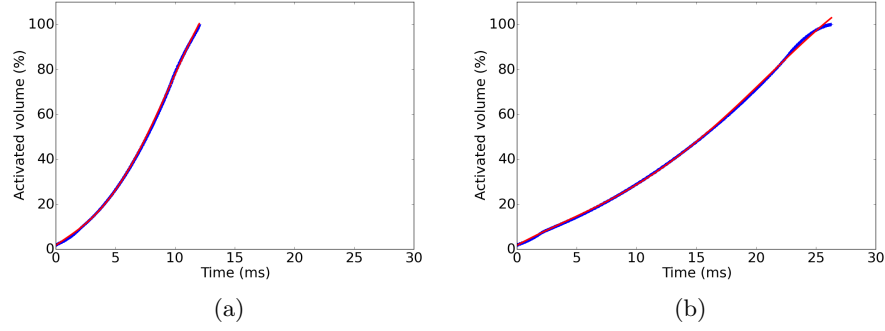


Fig. 3: Example of approximation of dependence the LV activated part from time using the 4-th degree polynomial; (a): $\gamma_0 = 0.0$, $\gamma_1 = 1.0$ (b): $\gamma_0 = 5.0$, $\gamma_1 = 7.0$

$$\begin{aligned}
 V_{\text{act}}(t) = & t^4(-0.0492\gamma_0\gamma_1 + 0.0013\gamma_0 + 0.0442\gamma_1 - 0.0056) + \\
 & t^3(1.1161\gamma_0\gamma_1 - 0.0487\gamma_0 - 1.0192\gamma_1 + 0.1559) + \\
 & t^2(-5.1988\gamma_0\gamma_1 + 0.5706\gamma_0 + 4.7070\gamma_1 - 1.0035) + \\
 & t(12.9829\gamma_0\gamma_1 - 0.8279\gamma_0 - 11.8881\gamma_1 + 4.7832) + \\
 & 1.6822
 \end{aligned} \tag{3}$$

There are two ways to verify the obtained results. For the first method, the researchers can measure the real shape and the activation map of a mammalian heart. After that, they can run the simulation with the parameters of the measured shape and obtain the activation map. These results can be used for the verification of the dependence we obtained. The second method of the verification is similar to the first, but the researchers can use data from the electrophysiological study.

Inverse functions cannot be obtained for the deduced formulas in strictly mathematical terms. Nevertheless, with the activation map data, the result still can be used for creating hypotheses about the fiber direction. Thus, we can construct the anatomical model [3].

5 Related Work

The usage of statistical processing of the patients clinical data is widespread in medicine [5]. Our research differs from them by using numerical experiments with mathematical models instead of clinical data.

The parameters similar to $V_{\text{act}}(t)$ is used in work [7]. Authors of this work use volume of activated myocardium as intermediate equation in mathematical transformation.

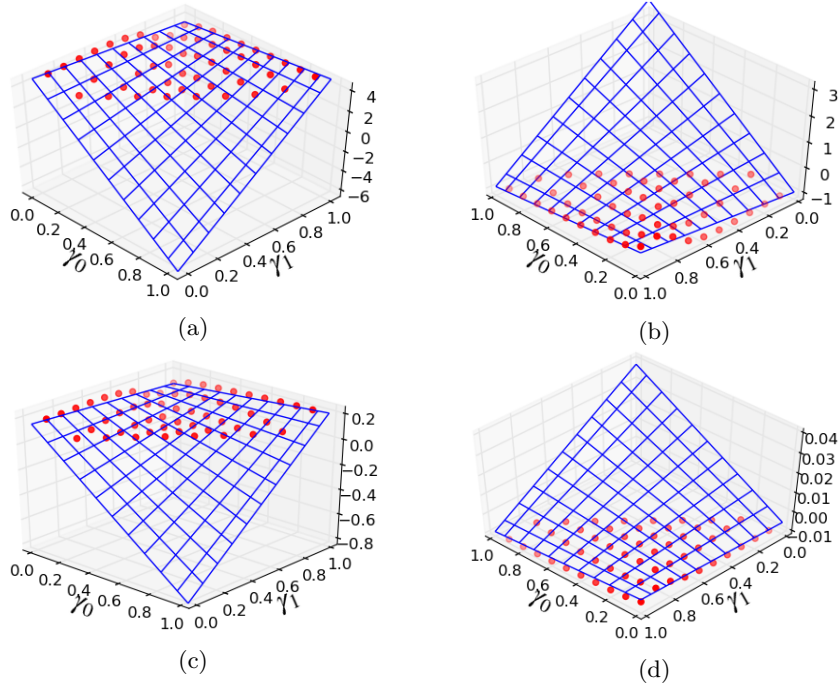


Fig. 4: Approximation of the coefficients p_0, p_1, p_2, p_3 with polynomial $B_3^i \gamma_1 \gamma_0 + B_2^i \gamma_1 + B_1^i \gamma_0 + B_0^i$. Images (a), (b), (c), and (d) correspond to coefficients B_0, B_1, B_2, B_3 , respectively.

Large number of experiments for dependencies research is used in paper [2]. The authors of this paper studied structural differences in the myocardium of different mammal species. In our work we are focused on another physiological problem and suggest technical implementation of its decision.

6 Conclusion

We presented an approach to study the dependency of computational model on parameters that is based on an execution of large amount of simulations with different parameter values on the HPC cluster. To derive dependencies between functional characteristics of simulated system and parameters, the statistical analysis of simulation results is used.

To provide an example of application of our approach to living system modeling, we studied the dependence of the dynamics of activated myocardium part during excitation on the model parameters of the myocardial fiber orientation in the ventricular wall.

Future works include a study of the dependencies between geometric and electrophysiological parameters of the LV to the dynamics of spiral waves.

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